

## CLAIMS

1. A microarray hybridization device which comprises:  
a flat substrate having a surface to which a microarray of reactive moieties can be attached,

liquid barrier means juxtaposed with said surface to create a chamber in which said microarray is located, and

means closing said chamber so said device may be manipulated without loss of liquid target solution that fills said chamber except for a gaseous bubble included therein,

said barrier means having inwardly facing surfaces which border said chamber, which surfaces are formed with a plurality of bubble-fracturing elements that extend laterally into said chamber so that, when said device is moved so that a liquid target solution in said chamber moves along said surface from one boundary of said chamber to another boundary, a bubble initially in said chamber is ruptured into a plurality of microbubbles that then assure very effective distribution of the liquid target solution in said chamber across the entire microarray, driven by movement of said microbubbles.

2. The microarray hybridization device of claim 1 wherein said cover is flat and is spaced uniformly from said surface by said barrier means.

3. The microarray hybridization device of claim 2 wherein said cover is made of substantially rigid, transparent material.

4. The microarray hybridization device of claim 2 wherein said barrier means has a height such as to space said cover about 0.2 and about 2 mm from said surface.

5. The microarray hybridization device of claim 2 wherein said barrier means forms a generally rectangular perimeter of said chamber and wherein one or more of the four walls of said barrier means includes sharp edges that are aligned substantially perpendicular to said surface upon which the microarray is attached, which edges are spaced apart by pockets and function as said bubble-fracturing elements.

6. The microarray hybridization device according to claim 5 wherein said bubble-fracturing elements are disposed along two opposed boundary walls of said rectangular perimeter barrier and are formed by a plurality of generally triangular fingers that project from boundary walls into said chamber and have said sharp edges at the tips thereof, with said pockets being located therebetween.

7. The microarray hybridization device according to claim 5 wherein said rectangular perimeter includes two longer walls and two shorter walls with said bubble-fracturing elements being formed as part of said two shorter walls.

8. The microarray hybridization device according to claim 7 wherein said triangular fingers in said two shorter walls are aligned so as to project in the direction from which bubbles in the target solution in said chamber will normally approach the respective wall when the device moved during hybridization.

9. The microarray hybridization device according to claim 2 wherein said bubble-fracturing elements are formed of hydrophobic material.

10. The microarray hybridization device according to claim 2 wherein said cover is made of an opaque hydrophobic material and includes at least one filling port through which said liquid target solution can be supplied into said chamber wherein a microarray is disposed.

11. A microarray hybridization device which comprises:  
a flat substrate having an upper surface,  
a microarray of reactive moieties attached to said upper surface,  
a liquid perimeter barrier juxtaposed with said surface to create a chamber in which said microarray is located, and

a cover juxtaposed with said barrier to close said chamber so said device may be manipulated without loss of liquid target solution that fills said chamber except for a gaseous bubble included therein,

said perimeter barrier having inwardly facing walls which border said chamber, which walls are formed with a plurality of bubble fracturing elements that extend laterally into said chamber so that, when said device is moved so that the liquid target solution moves along said surface upon which said microarray is located, a bubble initially in said chamber is ruptured into a plurality of microbubbles that assure very

effective distribution of a liquid target solution in said chamber across the entire microarray, driven by movement of said microbubbles.

12. The microarray hybridization device of claim 11 wherein said cover is flat, being made of substantially rigid, transparent material, and is spaced uniformly about 0.2 and about 2 mm from said surface by said perimeter barrier.

13. The microarray hybridization device of claim 12 wherein said perimeter barrier forms a generally rectangular chamber and wherein one or more of the four walls thereof includes protrusions having sharp edges that are aligned substantially perpendicular to said surface on which said microarray is located, said protrusions being spaced apart by pockets and functioning as said bubble-fracturing elements.

14. The microarray hybridization device according to claim 12 wherein said cover includes at least one filling port through which said liquid target solution can be supplied into said chamber and wherein said microarray includes a plurality of 3D spots which are attached to said upper surface and extend upward therefrom at least about 20  $\mu\text{m}$ , which 3D spots carry said reactive moieties.

15. A cover and gasket subassembly for forming a microarray hybridization device with a substrate having a microarray on a surface thereof, which subassembly comprises:

a flat cover having an upper and lower surface,  
a perimeter barrier of rectangular shape affixed to said lower surface of said cover,

pressure-sensitive adhesive upon an undersurface of said perimeter barrier for attachment of said cover to the surface of the substrate so as to surround the microarray, and

a release sheet covering said adhesive,  
said barrier having inwardly facing surfaces which border said chamber, which surfaces are formed with a plurality of bubble-fracturing elements that extend laterally into said chamber so that, when said device is moved so that a liquid target solution in said chamber moves along said surface from one boundary of said chamber to another boundary, a bubble initially in said chamber is ruptured into a plurality of microbubbles.

16. The subassembly of claim 15 wherein a removal tab is affixed to said upper surface of said flat cover and facilitates its removal from the substrate.

17. The subassembly of claim 16 wherein said cover and said tab are made of flexible material.

18. A method of effecting hybridization between probes and a target solution, which method comprises:

providing a flat substrate having a surface to which a microarray of reactive probe moieties are attached,

juxtaposing a perimeter liquid barrier with said surface to create a chamber, in which said microarray is located, and closing said chamber so said substrate may be manipulated without loss of liquid target solution,

filling said chamber with a target solution and a gaseous bubble, and

moving said substrate to cause the target solution to move from one boundary of said chamber to another with at least one such boundary being shaped so that as a result of such movement the bubble in said chamber is ruptured into a plurality of microbubbles that then assure very effective distribution of the liquid target solution across the entire microarray, driven by subsequent movement of such microbubbles.

19. The method of claim 18 wherein said chamber is formed and closed by a flat cover and a depending perimeter gasket that spaces said cover uniformly from said surface.

20. The method of claim 19 wherein said gasket forms a generally rectangular perimeter of said chamber having two opposed shorter walls and wherein said microbubbles are created by sharp-edged protrusions that project into said chamber from said two opposed shorter walls in the direction from which a bubble would approach each said wall during normal movement.

21. The method according to claim 20 wherein said target solution is introduced through at least one filling port in said cover which is then sealed.

22. The method of claim 20 wherein said substrate is moved by rotation about

an axis which is substantially horizontal and wherein said chamber is aligned so that said shorter walls are generally perpendicular to a line extending radially from said axis of rotation.